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Magnetic resonance imaging findings in probable Creutzfeld-Jacob disease: comparison with electroencephalography and cerebrospinal fluid characteristics

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Abstract

Background: Creutzfeld-Jacob disease (CJD) is a rare, progressive disease that has a vast clinical manifestation range. Cranial magnetic resonance imaging (MRI), electroencephalography (EEG), and measurement of 14-3-3 in cerebrospinal fluid (CSF) may offer a pragmatic approach in the diagnosis of CJD as an alternative to histopathological confirmation.
Purpose: To present the symptoms and signs of the CJD patients in regard to radiological and neurophysiological findings.
Material and Methods: We collected all cases with the diagnosis of probable CJD admitted to our neurology department between June 2010 and June 2014. The medical records and laboratory data, clinical features, results of MRI (including diffusion weighted images), EEG and CSF evaluations, and other laboratory data to exclude other possible diagnoses were recorded. None of the patients underwent biopsy or autopsy for histological diagnosis.
Results: Of 20 patients, 11 (55%) were men and nine (45%) were women. The mean age at disease onset was 60.0 ± 9.5 years (age range, 47–80 years). All patients without exception had characteristic abnormalities in DWI and/or FLAIR on admission, about 4 months after the initial symptom. Periodic complexes on EEGs characteristic for CJD were detected only in 10 patients (50%) on admission and in 13 patients (65%) during disease course. Out of 14 patients who underwent CSF examination, 11 (78.5%) were positive for 14-3-3 protein.
Conclusion: Although the definite diagnosis of CJD is made histopathologically, we aimed to discuss the value of magnetic resonance imaging in the diagnosis of CJD in respect to EEG findings and protein 14-3-3 levels in CSF.

Keywords
Creutzfeld-Jacob disease, magnetic resonance imaging (MRI), electroencephalography, cerebrospinal fluid examination, protein 14-3-3

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Introduction

Creutzfeldt-Jakob disease (CJD) is a rare disease, presenting as a rapidly progressive dementia (RPD) making up to approximately 85% of the human prion diseases (1). Although the definitive diagnosis is only possible via histopathological examination by autopsy or biopsy material, it is not only impractical, but also problematic due to specimen collection and exposure risk to the healthcare professionals (2). Other diagnostic tests including magnetic resonance imaging (MRI), electroencephalography (EEG), and measurement of 14-3-3 in cerebrospinal fluid (CSF) may offer a more pragmatic approach in the differential diagnosis of RPD. Brain MRI findings have also been incorporated

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in the new diagnostic CJD criteria that have recently been proposed (3). Here the clinical presentations and disease courses, MRI findings, and EEG and CSF examinations of 20 patients diagnosed as probable CJD are compared in terms of clinical utility aiding CJD diagnosis.

Material and Methods

We collected all cases with the diagnosis of probable CJD admitted to our neurology department between June 2010 and June 2014. All patients or their proxies gave informed consent for research and publication rights. The medical records and laboratory data, clinical features, results of MRI (including diffusion-weighted imaging [DWI]), EEG and CSF evaluations, and other laboratory data to exclude other possible diagnoses were recorded. None of the patients underwent biopsy or autopsy for histological diagnosis.

All patients were imaged on 1.5 T MRI scanners including T1, T2, fluid attenuated inversion recovery (FLAIR) and DWI sequences; these images were evaluated by one neuroradiologist blinded to the clinical presentation of the patients. Electroencephalogram was recorded in all patients via international 10-20 system for positioning of the electrodes and with double banana method. They were interpreted by neurologists specializing in epilepsy, who were blinded to the possible diagnosis. CSF examinations could be performed in 14 patients only, and included glucose, total protein, albumin, electrolytes, lactate dehydrogenase, cell count, gram staining, routine culture, cytological studies, 14-3-3 protein, oligoclonal bands, IgG index, and autoimmune and paraneoplastic antibodies.

Results

A total of 20 patients were evaluated, 11 (55%) were men and nine (45%) were women. The mean age at disease onset was 60.0 ± 9.5 years (age range, 47–80 years). The mean time between initial symptoms and admission was 3.7 ± 3.2 months. The initial symptom was rapidly progressive dementia in six cases (30%), though all patients had RPD during disease course eventually. Myoclonus was present in five patients (25%) on admission. In four patients (20%), hallucinations were present, and it was one of the initial symptoms in one patient. Only one patient presented with problems in higher cortical functions as visuospatial impairment and acalculia.

All patients without exception had characteristic abnormalities in DWI and/or FLAIR on admission – with a mean of 4 months after the initial symptoms (Fig. 1). In 11 patients (55%), both cortical ribboning and pulvinar sign were present (with hockey stick sign in one patient); seven patients (35%) showed cortical ribboning and two patients (10%) had pulvinar sign only. The distribution of cortical regions affected showed that frontal cortex and insula were involved in 11 patients (55%), occipital cortex was involved in eight patients (40%), and parietal cortex was involved in three patients (15%).

Periodic complexes on EEGs characteristic for CJD were detected only in 10 patients (50%) on admission and in 13 patients (65%) during disease course. Out of 14 patients who underwent CSF examination, 11 (78.5%) were positive for 14-3-3 protein. The mean disease duration was 11.8 ± 5.8 months (range, 5–19 months). Except three patients, all patients died due to secondary complications of infectious origin (two patients are still alive and we have lost contact with one patient).

Discussion

MRI is a relatively new modality used in the diagnosis of CJD, and is clearly becoming more important with more advanced techniques in differential diagnosis of neurodegenerative diseases and dementias with highly informative structural, functional and molecular changes underlying the corresponding pathology (4,5). The sensitivity and the specificity of DWI sequences were reported as high as 86% and 92%, respectively (6). Periodic sharp and slow wave complexes on EEG, on the other hand, have a sensitivity of 66% and specificity of 74% (7); they are not pathognomonic and may occasionally occur in other neurodegenerative diseases (8). In our study, typical EEG findings were observed in 13 out of 20 patients (65%), while all of our patients (100%) had MRI lesions in DWI sequences characteristic of CJD. Moreover, DWI sequences could detect the abnormalities as early as in the third week of symptom duration, before the appearance of periodic triphasic waves on EEG (9). Cerebrospinal fluid 14-3-3 protein levels were reported to provide a moderate accuracy in diagnosis of CJD with sensitivity of 92% and specificity of 80% (10). CSF samples were obtained in 14 patients in our study, and 11 of them (78.5%) were positive for 14-3-3. Typical characteristics of CJD in diffusion-weighted MRI therefore seems to be more useful than the CSF protein 14-3-3.

DWI is the most sensitive neuroimaging study for the early detection of CJD; which reveals characteristic findings including basal ganglia hyperintensities with diffusion restriction, hyperintensity of frontal, temporal, occipital, insular, and/or parietal regions referred to as cortical ribboning, symmetrical hyperintensity in the pulvinar nuclei of the thalamus (pulvinar sign), and/or symmetrical hyperintensity both in the pulvinar and

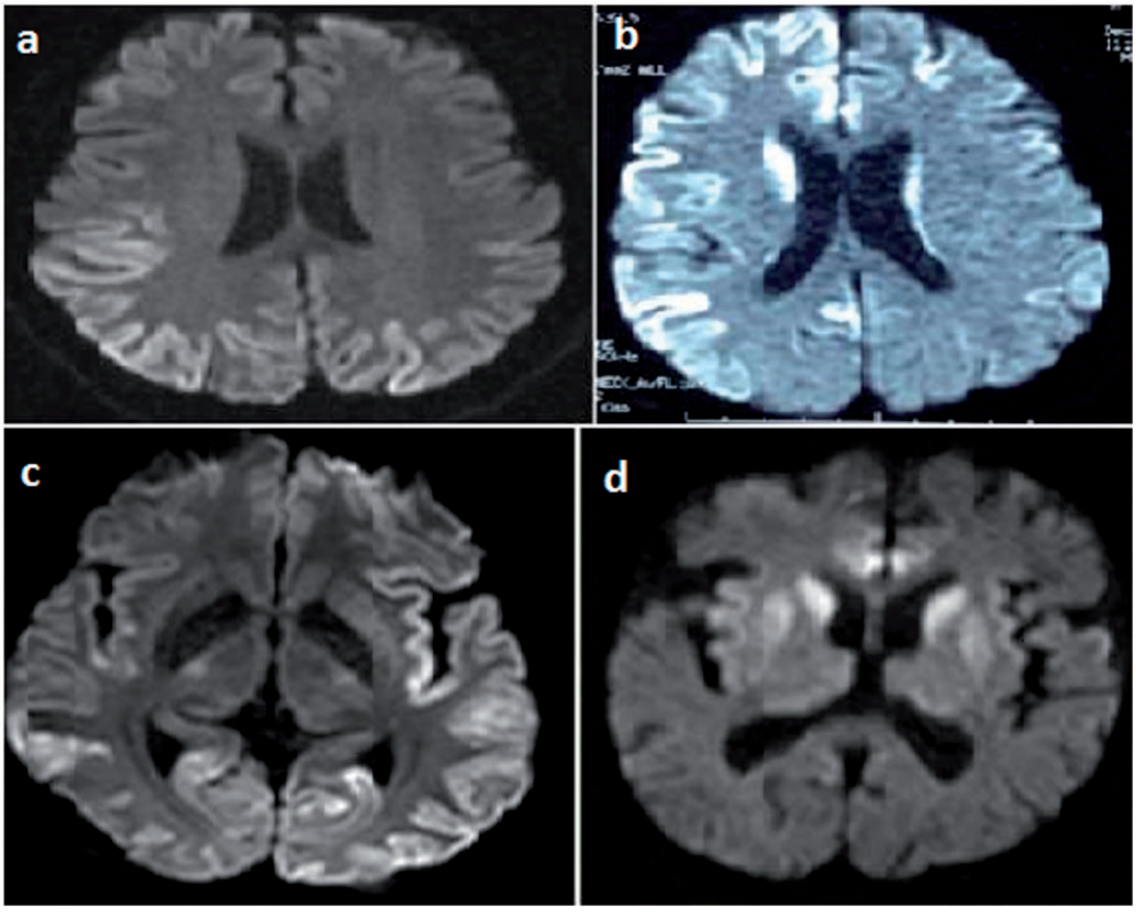

Fig. 1. Examples of diffusion- or FLAIR-weighted cranial magnetic resonance imaging (MRI) characteristics for CJD, showing cortical ribboning (a, b, c) and pulvinar sign (b, d); MRI was obtained 4 months after the onset of initial symptom in patients represented as (a) and (d), and 3 months after in patients represented as (b) and (c).

in dorsomedial thalamic nuclei (''hockey stick'' sign) (3,11–13). DWI findings should therefore be incorporated in the diagnosis of CJD, accurately differentiating it from other rapidly progressive dementia with a very high sensitivity and specificity.

These changes observed in neuroimaging studied are attributed to the accumulation of abnormal vacuoles in the cytoplasm and the microvacuolation of neuritic processes heralding spongiform degeneration, neuronal loss and gliosis (14). Spongiform changes in CJD on histology are patchy in nature, for which histopathological examination by autopsy or biopsy material therefore requires wide sampling of brain tissue. We shall not undervalue the importance of histopathological examination in the definitive diagnosis of CJD; however, problems related with the feasibility of the procedure, specimen collection and exposure risk to the healthcare professionals make it difficult and impractical for most of the neurology centers.

In conclusion, our study demonstrated that the DWI allows easy and early identification of pathological changes and should therefore be included in the work-up of every patient with RPD. These MRI observations and pathological changes might provide structural correlate for the electrophysiological changes and may be used as a non-invasive tool in the diagnosis of CJD, together with clinical and other laboratory data.

Conflict of interest

None declared.

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